Cystic Fibrosis

Cystic Fibrosis is an autosomal recessive genetic disorder characterized by severe lung damage and nutritional deficiencies. Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene causes the body to produce thick, sticky secretions that obstruct passageways in the lungs and pancreas leading to:

- Lung infections and respiratory failure
- Blockage of pancreatic enzymes that lead to malnutrition
- Infertility in affected males

The most common mutation causing CF is a three-base pair deletion in the position of delta F508, but there are now over 700 mutations identified in the CFTR gene.

Newborn Screening — The identification of increased immunoreactive trypsinogen (IRT) levels in the blood of infants with CF has made neonatal screening for CF possible. Trypsinogen is one of the secretory products of the pancreas making its level in the blood a specific marker of pancreatic function. Detection of high levels of IRT in the newborn period place the infant at risk for CF. Although there is no cure, newborns screened for cystic fibrosis can benefit from early diagnosis and treatment, which can:

- Improve growth
- Improve lung function
- Reduce hospital stays
- Add years to life

While newborn screening is not a definitive diagnostic test for cystic fibrosis, it can lead to confirmatory sweat testing that can rule out or confirm a CF diagnosis. The Cystic Fibrosis Foundation and the Centers for Disease Control and Prevention recommend screening for cystic fibrosis for all newborns.

Estimated Prevalence in Missouri: 1: 4000

Analyte Measured: Immunoreactive Trypsinogen (IRT). Determination of (IRT) concentrations from dried blood spots serves as the basis for the Missouri Newborn Screening test for CF. IRT concentration is high in the blood of infants with CF, presumably from leakage of the protein into the circulation after exocrine pancreatic injury. Some infants that do not have CF may also have elevated levels of IRT in the newborn period, but these levels decrease to normal in the first weeks of life. Infants having persistently high IRT levels in the first weeks of life are considered at risk for CF. **Therefore, an elevated IRT level in a newborn screen will require a repeat screen collected after 7 days and prior to 6 weeks of life to determine if a persistent elevation is present.** An infant with a persistent IRT elevation needs to be referred to a certified CF Center for diagnostic sweat testing.

Reporting Ranges:

IRT ranges are age dependent:

Age at collection	Normal	Elevated (repeat sample requested at >7 days of life)	Diagnostic testing required at CF follow up center
≤ 7 days	< 85 ng/ml	≥ 85 ng/ml	Elevated initial and repeat screen
> 7 days	< 70 ng/ml	≥ 70 ng/ml	

Feeding Effect: None

Timing Effect: Because IRT concentration is frequently high immediately after birth; specificity is improved if the test is performed after the first day of life. A specimen collected between 24 and 48 hours of life is optimal. If the IRT is elevated in the initial screen, a repeat screen should be collected after seven days of life and before six weeks of life to determine persistent elevations of IRT. There is also an age-related decline in IRT levels in children with CF. IRT levels within the normal range will be considered non-interpretable after 3 months of age and will not be reported on the newborn screen.

Confirmation: All babies that demonstrate persistently elevated levels of IRT in the newborn screen should be referred for a sweat test (pilocarpine iontophoresis) at an accredited Cystic Fibrosis Center. The Missouri Department of Health and Senior Services have contracted four accredited CF Centers for follow-up sweat testing, counseling and consultation. These four centers are:

Cardinal Glennon Children's Hospital - St. Louis	314-268-6439
Children's Mercy Hospital – Kansas City	816-983-6628
St. Louis Children's Hospital – St. Louis	314-454-2353
University Hospital & Clinics – Columbia	573-884-8579

Treatment: To receive optimal treatment, children with CF should be examined by specialized CF centers that offer a comprehensive approach to CF care and that can closely monitor the development of respiratory infections and provide nutritional and psychosocial support. CF patients follow a strict regimen to treat the disease as well as care to reduce contracting outside infections. The treatment regimen can include:

- Oral and or IV Antibiotics to fight infections
- Vitamins to improve general health
- Respiratory therapy such as bronchodilators and other treatments to clean airways and dislodge mucus from the lungs
- Steroids to reduce inflammation
- Supplemental oxygen therapy

- Enzymes to aid in digestion
- Liquid nutrition or healthy high calorie diets for weight gain
- Counseling and support

Comment: The screening test for CF is meant to identify infants at risk for CF and in need of diagnostic sweat testing. A "normal" screen does not rule out the possibility of the disease. The health care provider should remain vigilant to detect CF among children with clinical symptoms. Also, mild or atypical forms of CF and babies with meconium ileus may not demonstrate elevated IRT levels in the newborn period.

Considerations:

- Premature or sick infants may have a false-positive screen due to increased stress on the body.
- Blood collection with EDTA can result in inaccurate screening results
- Babies with meconium ileus have an increased likelihood of having CF, but may not have elevated IRT levels in the newborn period

Reference and Support groups:
There are many on line information and support resources for Cystic Fibrosis. A few of them are listed here.

Cystic Fibrosis Foundation - www.cff.org
March of Dimes – www.marchofdimes.com
Medline Plus – www.nlm.nih.gov/medlineplus/cysticfibrosis.html
Cysticfibrosis.com – www.cysticfibrosis.com
Cystic Fibrosis Reaching Out Foundation – www.ReachingOutFoundation.org